REMARKS

Claims 1, 9, 30, 31 and 44 have been amended. Claim 45 has been amended to correct obvious typographical errors. Claims 42 and 43 have been cancelled without prejudice or disclaimer. Now pending in the application are claims 1-7, 9-18, 20-31, 33-35, 37, 39-41 and 44-49. No new matter has been added.

Amendment or cancellation of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicants make these amendments without prejudice to pursuing the original subject matter of this application in a later filed application claiming benefit of the instant application, including without prejudice to any determination of equivalents of the claimed subject matter.

Rejections under 35 USC 112, first paragraph

Claims 30, 31, 33-35, 37 and 39-43 have been rejected under 35 U.S.C. § 112, first paragraph, because, in the Examiner's view, "[t]here is no teaching either in the specification or prior art that serotonin uptake and/or dopamine uptake inhibitors are either well known to have therapeutic utility in treating every known neurodegenerative disease, psychiatric disease, dopamine dysfunction, cocaine abuse and clinical dysfunctions or efficacious in known animal models of every known neurodegenerative disease, psychiatric disease, dopamine dysfunction, cocaine abuse and clinical dysfunctions."

Applicants respectfully disagree. As an initial matter, Applicants note that the claims, as amended, do not recite the language "clinical dysfunction," thus mooting any objection to this language.

Furthermore, as explained in the present specification, modulators of dopamine or serotonin uptake are useful in treatment of many conditions. To cite just one example, "[i]nhibition of 5-hydroxytryptamine reuptake has an effect on diseases mediated by 5HT receptors. Compounds that provide such inhibition can be useful, for example, as therapeutic anti-depressants" (Specification at page 7, lines 7-9).

One of ordinary skill in the art can readily determine which conditions can be treated according to the methods of the invention. For example, as the Examiner has correctly acknowledged, the compounds of the invention bind to monoamine transporters such as the dopamine transporter (DAT) and/or serotonin transporter (SERT), and one of ordinary skill in the art would know that conditions related to the DAT and/or SERT (including, e.g., dopamine dysfunctions) can be treated according to the present methods.

In addition, Applicants point out that the specification need not teach that serotonin and/or dopamine reuptake inhibitors are effective for the treatment of "every known neurodegenerative disease, psychiatric disease, dopamine dysfunctions, cocaine abuse and clinical dysfunctions," as the Examiner has stated. Applicants contend that what is required is that the scope of enablement be commensurate with the scope of the claims (se, e.g., MPEP 2164.05). Applicants contend that the scope of enablement provided amply supports the pending claims.

Even further, as discussed in Applicants' previous submission, not all of the rejected claims recite the language to which the Examiner has objected. The Examiner does not appear to have addressed these claims in the present Office Action.

For example, claim 39 (and claim 40 which depends therefrom) is directed to a method of treating *dopamine related* dysfunction. As previously pointed out, the present compounds are inhibitors of the dopamine transporter and/or serotonin transporter, and Applicants respectfully contend that the method of claim 39 is amply enabled by the teachings of the present specification.

Claim 41 is directed to a method for treating *cocaine abuse*. As described in the specification (e.g., at page 7, lines 10-13), cocaine recognition sites are localized on monoamine transporters, and, therefore, compounds which inhibit the DAT are useful for the treatment of cocaine abuse. Applicants respectfully contend that the method of claim 41 is amply enabled by the teachings of the present specification.

Reconsideration and withdrawal of this rejection is proper and the same is requested.

Rejections under 35 USC 112, second paragraph

Claim 1 was rejected as indefinite; the Examiner stated that "it is not clear whether only X1 . . . is part of the ring or whole C=CX1Y is part of the ring." Office Action at Section 8. Claim 1 has been amended to clarify that when X is NR_3 or NSO_2R_3, then the N atom is a member of the ring, and when X is $C=CX_1Y$, the C atom is a member of the ring. Applicants respectfully contend that claim 1 as presently pending is fully compliant with the requirements of 35 USC 112. Reconsideration and withdrawal of the rejection is requested.

As Applicants understand the rejection, claim 9 was rejected as indefinite for reciting the language "X is N." Claim 9 has been amended to provide that, in the embodiment of claim 9, X is NR_3 or NSO_2R_3. Applicants respectfully contend that claim 9 is fully compliant with the requirements of 35 USC 112. Reconsideration and withdrawal of the rejection is requested.

Claim 44 was rejected as unclear; the Examiner asked, "what is being claimed?" Claim 44 has been amended to recite that the claim is directed to a compound having the structure shown. The Examiner also objected to the language "protecting group" in claim 44. Applicants respectfully disagree. The term "protecting group" is art-recognized and one of ordinary skill in the art would have no difficulty in understanding the term "protecting group." Moreover, the present specification provides, e.g., at pp. 14-15, a large number of protecting groups. Applicants respectfully contend that claim 44 is fully compliant with the requirements of 35 USC 112. Reconsideration and withdrawal of the rejection is requested.

Claims 25-28, 30, 31, and 42 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite.

As to claims 25-28, the Examiner appears to contend that the language "inhibiting 5-hydroxytryptamine reuptake of a monoamine transporter" is unclear. Further, the Examiner apparently takes the position that "inhibiting serotonin uptake" and "inhibiting serotonin transporter" are the same thing.

Applicants respectfully disagree. Claim 25 provides a method for inhibiting 5-hydroxytryptamine reuptake by contacting the monoamine transporter with a monoamine transporter inhibitor compound of the present invention. Claim 26 is directed to preferred monoamine transporters which include the dopamine transporter, the serotonin transporter and the norepinephrine transporter. Claim 27 is directed to a method for inhibiting 5-hydroxytryptamine reuptake of a monoamine transporter in a mammal comprising administering to the mammal a 5-hydroxytryptamine reuptake. Claim 28 is directed to a method for inhibiting dopamine reuptake of a dopamine transporter in a mammal.

Applicants contend that the term "inhibiting 5-hydroxytryptamine reuptake of a monoamine transporter" in claims 25-28 is clear on its face and would be clear to one of ordinary skill in the art. None of the claims contains the exact language referenced by the Examiner: "inhibiting serotonin uptake" and "inhibiting serotonin transporter"; therefore, Applicants must disagree with the Examiner's statement that "applicants did not address the issue of difference between inhibiting serotonin uptake and inhibiting serotonin transporter." Applicants have addressed this issue by pointing out that the language "inhibiting serotonin transporter" does not appear in the pending claims; thus, Applicants urge that the issue is moot. Applicants respectfully submit that the claims are clear and are not indefinite.

As to the Examiner's questions about how the transporters are contacted, Applicants submit that claims 25 and 26 are not limited to either *in vitro* or *in vivo* inhibition of 5-hydroxytryptamine reuptake of a monoamine transporter, while claims 27 and 28 recite the administration of a compound to a mammal.

As to claims 30, 31 and 42, the Examiner states that "[a]ccording to applicants arguments, clinical dysfunction covers every possible known disease in the art." Applicants respectfully disagree, as discussed in a previous response. However, for the purposes of expediting prosecution, and as noted above, the claims as amended no longer recite this language.

Reconsideration and withdrawal of the rejections is proper and the same is requested.

Rejections under 35 USC 102

Claims 1-29, 41, 44, and 45 have been rejected under 35 USC § 102(a) as anticipated by Meltzer *et al.*, *J. Med. Chem.* 2001, 44, 2619-1635. This rejection is traversed. As previously noted, the Meltzer *et al.* paper cited by the Examiner is the work of the present inventors, published less than one year prior to the present application for patent, and accordingly cannot be cited against the present claims. If required, an appropriate Declaration by the Applicants will be supplied.

Reconsideration and withdrawal of this rejection is proper and the same is requested.

Applicants note with appreciation that the previous rejection of claims under 35 U.S.C. § 102(b) as anticipated by Zhao *et al.* (J. Med Chem. 2000), has been withdrawn. However, the Examiner has now cited this reference against claims 46-49. This rejection is traversed.

The Zhao reference describes certain tropane analogs having substitution at the C6 or C7 positions of the tropane ring system, but Zhao does not teach or suggest the compounds or methods of the presently-pending claims. The Examiner points to compounds 16 and 28 of Zhao as anticipating claims 46-49, but compounds 16 and 28 of Zhao each include a carbon-carbon double

bond in the ring system, unlike the compounds of claims 46-49, in which the ring system does not contain any carbon-carbon double bonds. Thus, Zhao does not teach or suggest the compounds of pending claims 46-49. Accordingly, reconsideration and withdrawal of the rejection is appropriate and the same is requested.

Certain of the pending claims have been rejected under 35 U.S.C. 102(b) by Meltzer *et al.*, WO 99/02526. Applicants cannot determine which claims are rejected, as the Examiner has merely stated that "this reference still anticipates the instant claims when R1 represents –COR3 and R2 represents –OH group in the compounds of formulae I, II and III (see pages 7-8 and claim 1 [of Meltzer WO 99/02526])." Assuming *arguendo* that the Examiner intends the rejection to apply to all pending claims, Applicants provide the following remarks.

The Meltzer WO 99/02526 reference describes tropanes and tropane analogs, but this reference does not teach or suggest the presently-claimed compounds or methods for using them. For example, as to claims 46-49, the portions of the Meltzer WO 99/02526 reference cited by the Examiner (e.g., formulae I, II and III of Meltzer WO 99/02526) do not teach or suggest compounds having an oxo (=O) group at the 6- or 7-position of the ring system. Thus, the Meltzer WO 99/02526 reference cannot anticipate claims 46-49. Furthermore, the broad structural formulae to which the Examiner refers cannot anticipate the presently-claimed compounds (and methods of use thereof, and pharmaceutical compositions thereof) according to pending claims 1-7, 9-18, 20-31, 33-35, 37, 39-41 and 44-45. As provided by the MPEP, an earlier broader disclosure does not anticipate a later, more specifically-drawn claim to compounds within that genus (absent circumstances not applicable here, see, e.g., MPEP 2131.02 and 2144.08(II)(A)(4)(a)). Applicants respectfully contend that the Meltzer WO 99/02526 reference does not anticipate, nor does it teach or suggest, the claimed compounds and compositions (and methods of use thereof) as defined by the pending claims. Accordingly, reconsideration and withdrawal of the rejection is appropriate and the same is requested.

Claims 1-45 have been rejected under 35 U.S.C. 102(e) as being anticipated by Meltzer (US 6,353,105; "Meltzer '105"). As with the rejection over the Meltzer WO 99/02526 reference discussed above, Applicants cannot determine which claims are rejected, as the Examiner has merely stated that "[Meltzer '105] still anticipate[s] the instant claims when R1 represents –COR3 and R2 represents OH group in compounds of formulae I, II and III." Assuming *arguendo* that the Examiner intends the rejection to apply to all pending claims, Applicants provide the following remarks.

The Meltzer '105 patent (which corresponds to the Meltzer WO 99/02526 reference discussed *supra*) describes tropanes and tropane analogs, but this reference does not teach or suggest the presently-claimed compounds or methods for using them. For example, as to claims 46-49, the portions of the Meltzer '105 patent cited by the Examiner (e.g., formulae I, II and III of Meltzer '105) do not teach or suggest compounds having an oxo (=O) group at the 6- or 7-position of the ring system. Thus, the Meltzer '105 reference cannot anticipate claims 46-49. Furthermore, the broad structural formulae to which the Examiner refers cannot anticipate the more-specifically-drawn compounds (and methods of use thereof, and pharmaceutical compositions thereof) according to pending claims 1-7, 9-18, 20-31, 33-35, 37, 39-41 and 44-45. As described above, an earlier broader disclosure does not anticipate a later, more specifically-drawn claim to compounds within that genus (absent circumstances not applicable here, see, e.g., MPEP 2131.02 and 2144.08(II)(A)(4)(a)). Applicants respectfully contend that the Meltzer '105 patent does not anticipate, nor does it teach or suggest, the claimed compounds and compositions (and methods of use thereof) as defined by the pending claims. Accordingly, reconsideration and withdrawal of the rejection is appropriate and the same is requested.

Claims 1-45 have been rejected under 35 U.S.C. § 102(e) as anticipated by Meltzer (US 6,670,375; "Meltzer '375"). As with the rejection over the Meltzer '105 patent reference discussed above, Applicants cannot determine which claims are rejected, as the Examiner has merely stated that "[Meltzer '375] still anticipate[s] the instant claims when R1 represents –COR3 and R2 represents OH group in compounds of formulae I, II and III." Assuming *arguendo* that the

Examiner intends the rejection to apply to all pending claims, Applicants provide the following remarks.

The Meltzer '375 patent (which corresponds to the Meltzer WO 99/02526 reference and Meltzer '105 patent discussed *supra*) describes tropanes and tropane analogs, but this reference does not teach or suggest the presently-claimed compounds or methods for using them. For example, as to claims 46-49, the portions of the Meltzer '375 patent cited by the Examiner (e.g., formulae I, II and III of Meltzer '375) do not teach or suggest compounds having an oxo (=O) group at the 6- or 7-position of the ring system. Thus, the Meltzer '375 reference cannot anticipate claims 46-49. Furthermore, the broad structural formulae to which the Examiner refers cannot anticipate the more-specifically-drawn compounds (and methods of use thereof, and pharmaceutical compositions thereof) according to pending claims 1-7, 9-18, 20-31, 33-35, 37, 39-41 and 44-45, as described above with respect to the '105 patent. Applicants respectfully contend that the Meltzer '375 patent does not anticipate, nor does it teach or suggest, the claimed compounds and compositions (and methods of use thereof) as defined by the pending claims. Accordingly, reconsideration and withdrawal of the rejection is appropriate and the same is requested.

Applicants further note that, because the Meltzer '105 and '375 patents were owned by the same person or subject to an obligation of assignment to the same person at the time the present invention was made, these patents therefore cannot be used in a rejection under 35 U.S.C. 103(a) because those patents qualify as prior art, if at all, only under 35 U.S.C. 102(e)/(f)/(g). See 35 U.S.C. 103(c)(1).

Double Patenting Rejections

The Examiner has rejected claims 1-7, 9-18, 20-28, 44 and 45 under the judicially-created doctrine of obviousness-type double patenting over claims 1-11, 21, 22, 27 and 32 of the Meltzer '105 patent. The Examiner states that although the pending claims are not identical to the cited claims of the Meltzer '105 patent, "the instant claims are encompassed by broader values of

variables R1 and R2 in compounds of formulae I, II and III of the cited patent, specifically when R1 represents COR3 and R2 represents OH or OR3 group." This rejection is traversed.

As the Examiner is aware, present claim 1 is directed to compounds having the structure indicated, in which the R_1 group is COR_3. and R_2 is OH or O. Applicants urge that the presently-claimed compounds represent a patentably distinct invention with respect to the claimed invention of the '105 patent, in that the invention of present claim 1 is not an obvious variation on the invention of the claims of the '105 patent. Similarly, method claims 25, 27, and 28, and the claims dependent thereupon, which are directed to methods for using the compound of instant claim 1, are also patentably distinct over the claims of the '105 patent. Claim 29, directed to pharmaceutical compositions of a compound of claim 1, also is not an obvious variation on the invention of the claims of the '105 patent.

Even more, claims 2-7, 9-18, 20-24, and 44-45 further define the present invention and provide additional basis for patentable distinction over the claims of the '105 patent. For example, claims 23 and 24 are each directed to two compounds. Applicants contend that these compounds would not have been obvious in view of the claims of the '105 patent.

The Examiner has rejected claims 1-7, 9-18, 20-24, 29-31, 33-35, 37, and 39-45 under the judicially-created doctrine of obviousness-type double patenting over claims 1 and 3-22 of the Meltzer '375 patent. The Examiner states that although the pending claims are not identical to the cited claims of the Meltzer '375 patent, "the instant claims are encompassed by broader values of variables R1 and R2 in compounds of the cited patent, specifically when R1 represents COR3 and R2 represents OR3 group." This rejection is traversed.

As the Examiner is aware, present claim 1 is directed to compounds having the structure indicated, in which the R_1 group is COR_3. and R_2 is OH or O. Applicants urge that the presently-claimed compounds represent a patentably distinct invention with respect to the claimed invention of the '375 patent, in that the invention of present claim 1 is not an obvious variation on the

invention of the claims of the '105 patent. Similarly, method claims 29, 30,31, 33, 35, 39 and 41, and the claims dependent thereupon, which are directed to methods for using the compound of instant claim 1, are also patentably distinct over the claims of the '105 patent. Claim 29, directed to pharmaceutical compositions of a compound of claim 1, also is not an obvious variation on the invention of the claims of the '105 patent.

Even more, claims 2-7, 9-18, 20-24, and 44-45 further define the present invention and provide additional basis for patentable distinction over the claims of the '375 patent. For example, claims 23 and 24 are each directed to two compounds. Applicants contend that these compounds would not have been obvious in view of the claims of the '375 patent.

For at least the foregoing reasons, Applicants request reconsideration and withdrawal of the rejections.

CONCLUSION

It is respectfully submitted that this application is in condition for allowance. Early and favorable action is earnestly solicited.

The undersigned requests any extensions of time necessary for response. Although it is not believed that any additional fees are needed to consider this submission, the Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary, under Reference No. 56579 (70207), Customer No. 21874.

If the Examiner considers that issues remain, he is invited to contact the undersigned at the telephone number below.

Respectfully submitted,

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